

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|-------|------|--|--------------------|------------------|---------|------------------|
| S1 | 1 | ("6608026").PN. | US-PGPUB; USPAT | OR | OFF | 2004/11/09 13:59 |
| S2 | 28 | avpi | US-PGPUB; USPAT | OR | ON | 2004/11/09 13:51 |
| S3 | 314 | iap same apoptosis | US-PGPUB; USPAT | OR | ON | 2004/11/09 13:51 |
| S4 | 9 | S2 and S3 | US-PGPUB; USPAT | OR | ON | 2004/11/09 13:53 |
| S5 | 3 | S4 and (@pd<="20000929" or @rlad<="20000929") | US-PGPUB; USPAT | OR | ON | 2004/11/09 13:54 |

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|------------|---------|
| ENTRY | SESSION |
| 0.21 | 0.21 |

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DICTIONARY FILE UPDATES: 8 NOV 2004 HIGHEST RN 777024-10-9

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=> s avpi/sqep
      6 AVPI/SQEP
      63671 SQL=4
L1      6 AVPI/SQEP
      (AVPI/SQEP AND SQL=4)
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| => FIL CAPLUS MEDLINE EMBASE SCISEARCH BIOSIS COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---------------------|------------------|
| FULL ESTIMATED COST | 7.02 | 7.23 |

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L2      21 L1
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=> dup rem l2
PROCESSING COMPLETED FOR L2
L3      19 DUP REM L2 (2 DUPLICATES REMOVED)
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=> d l3 bib ab
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L3  ANSWER 1 OF 19  CAPLUS  COPYRIGHT 2004 ACS on STN
AN  2004:702118  CAPLUS
DN  141:218943
TI  Compositions and methods for enhancing apoptosis using BIR domain-binding
```

oligopeptides to release melanoma inhibitor of apoptosis protein from caspase

IN Fairbrother, Wayne J.; Deshayes, Kurt; Fischer, Saloumeh; Flygare, John A.; Franklin, Matthew C.; Vucic, Domagoj

PA Genentech, Inc., USA

SO PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | WO 2004072641 | A1 | 20040826 | WO 2003-US3799 | 20030207 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRAI WO 2003-US3799 20030207

OS MARPAT 141:218943

AB The present invention is directed to compns. of matter useful for the enhancement of apoptosis in mammals and to methods of using those compns. of matter for the same. BDB (BIR domain-binding) oligopeptides that specifically bind to ML-IAP (melanoma inhibitor of apoptosis) and release the inhibitory effect ML-IAP has on caspase activity are claimed. Apoptosis in cancer cells is increased by administering the oligopeptide.

=> d l3 bib ab 2-19

L3 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:722899 CAPLUS

DN 141:248727

TI Peptide compositions and methods for enhancing apoptosis

IN Deshayes, Kurt; Fairbrother, Wayne; Flygare, John; Franklin, Matthew C.; Fischer, Saloumeh; Vucic, Domagoj

PA Genentech, Inc., USA

SO U.S. Pat. Appl. Publ., 50 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|------|----------|-----------------|----------|
| PI | US 2004171554 | A1 | 20040902 | US 2003-364645 | 20030207 |
| PRAI | US 2003-364645 | | 20030207 | | |

OS MARPAT 141:248727

AB The present invention is directed to compns. of peptides useful for the enhancement of apoptosis in mammals and to methods of using those compns. of matter for the same.

L3 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:498222 CAPLUS

DN 141:169708

TI Structural Mining: Self-Consistent Design on Flexible Protein-Peptide Docking and Transferable Binding Affinity Potential

AU Liu, Zhijie; Dominy, Brian N.; Shakhnovich, Eugene I.

CS Department of Chemistry and Chemical Biology, Harvard University,

Cambridge, MA, 02138, USA

SO Journal of the American Chemical Society (2004), 126(27), 8515-8528
CODEN: JACSAT; ISSN: 0002-7863

PB American Chemical Society

DT Journal

LA English

AB A flexible protein-peptide docking method has been designed to consider not only ligand flexibility but also the flexibility of the protein. The method is based on a Monte Carlo annealing process. Simulations with a distance root-mean-square (dRMS) virtual energy function revealed that the flexibility of protein side chains was as important as ligand flexibility for successful protein-peptide docking. On the basis of mean field theory, a transferable potential was designed to evaluate distance-dependent protein-ligand interactions and atomic solvation energies. The potential parameters were developed using a self-consistent process based on only 10 known complex structures. The effectiveness of each intermediate potential was judged on the basis of a Z score, approximating the gap between the energy of the native complex and the average energy of a decoy set. The Z score was determined using exptl. determined native structures and decoys generated by docking with the intermediate potentials. Using 6600 generated decoys and the Z score optimization criterion proposed the developed potential yielded an acceptable correlation of $R^2 = 0.77$, with binding free energies determined for known MHC I complexes (Class I Major Histocompatibility protein HLA-A*0201) which were not present in the training set. Test docking on 25 complexes further revealed a significant correlation between energy and dRMS, important for identifying native-like conformations. The near-native structures always belonged to one of the conformational classes with lower predicted binding energy. The lowest energy docked conformations are generally associated with near-native conformations, less than 3.0 Å dRMS (and in many cases less than 1.0 Å) from the exptl. determined structures.

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:566939 CAPLUS

DN 141:253639

TI Structure-Based Design, Synthesis, and Evaluation of Conformationally Constrained Mimetics of the Second Mitochondria-Derived Activator of Caspase That Target the X-Linked Inhibitor of Apoptosis Protein/Caspase-9 Interaction Site

AU Sun, Haiying; Nikolovska-Coleska, Zanita; Yang, Chao-Yie; Xu, Liang; Tomita, York; Krajewski, Krzysztof; Roller, Peter P.; Wang, Shaomeng

CS Departments of Internal Medicine and Medicinal Chemistry and Comprehensive Cancer Center, University of Michigan, Ann Arbor, MI, 48109-0934, USA

SO Journal of Medicinal Chemistry (2004), 47(17), 4147-4150
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

AB A successful structure-based design of conformationally constrained second mitochondria-derived activator of caspase (Smac) mimetics that target the XIAP/caspase-9 interaction site is described. The most potent Smac mimetic (12d) has a K_i of 350 nM for binding to the XIAP BIR3 domain protein. The compound 12d is found to be effective in enhancing apoptosis induced by cisplatin in PC-3 human prostate cancer cells.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:434582 CAPLUS

DN 139:30774

TI Methods and compositions using peptidyl and nonpeptidyl compounds for

derepression of IAP-inhibited caspase, therapeutic use, and methods for identification of agents

IN Reed, John C.; Houghten, Richard A.; Nefzi, Adel; Ostresh, John M.;
Pinilla, Clemencia; Welsh, Kate
PA The Burnham Institute, USA; Torrey Pines Institute for Molecular Studies
SO PCT Int. Appl., 182 pp.
CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | WO 2003045974 | A2 | 20030605 | WO 2002-US37577 | 20021121 |
| | WO 2003045974 | A3 | 20040219 | | |
| | W: | | | | |
| | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, | | | | |
| | CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, | | | | |
| | GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, | | | | |
| | LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, | | | | |
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| | RW: | | | | |
| | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, | | | | |
| | KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, | | | | |
| | FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, | | | | |
| | CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 2003180805 | A1 | 20030925 | US 2002-302811 | 20021121 |
| | EP 1465649 | A2 | 20041013 | EP 2002-793997 | 20021121 |
| | R: | | | | |
| | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |
| | IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |

PRAI US 2001-331957P P 20011121
WO 2002-US37577 W 20021121

AB The invention provides isolated agents having a core peptidyl or nonpeptidyl (e.g. urea derivative, diketopiperazine derivative) structure, wherein

the agent derepresses an IAP-inhibited caspase. The invention also provides a method of derepressing an IAP-inhibited caspase. The method consists of contacting an IAP-inhibited caspase with an effective amount of an agent to derepress an IAP-inhibited caspase. The methods of the invention can be used for promoting apoptosis in a cell and for reducing the severity of a pathol. (e.g. cancer) characterized by reduced levels of apoptosis. Methods for identifying agents that derepress an IAP-inhibited caspase are also provided.

L3 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:376888 CAPLUS

DN 138:379183

TI Methods and reagents for peptide-BIR interaction screens

IN Boudreault, Alain; Korneluk, Robert G.; La Casse, Eric; Liston, Peter

PA Aegera Therapeutics, Inc., Can.

SO PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | WO 2003040172 | A2 | 20030515 | WO 2002-CA1738 | 20021112 |
| | WO 2003040172 | A3 | 20040311 | | |
| | W: | | | | |
| | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, | | | | |
| | CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, | | | | |
| | GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, | | | | |
| | LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, | | | | |
| | PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, | | | | |
| | TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, | | | | |
| | MD, RU, TJ, TM | | | | |

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

US 2003157522 A1 20030821 US 2002-293371 20021112
PRAI US 2001-332300P P 20011109
US 2002-370934P P 20020408

AB The invention features a substantially pure polypeptide having a length of less than 100 amino acids and capable of forming a complex with a polypeptide that includes a BIR domain. The invention also features displacement assays in which the ability of a candidate compound to disrupt the interaction between a BIR domain-containing polypeptide and a polypeptide of the invention is indicative of the ability of the candidate compound to modulate IAP biol. activity.

L3 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:833884 CAPLUS

DN 139:317425

TI Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis

IN Debatin, Klaus Michael; Fulda, Simone

PA Deutsches Krebsforschungszentrum Stiftung des Oeffentlichen Rechts, Germany

SO Eur. Pat. Appl., 19 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | EP 1354952 | A1 | 20031022 | EP 2002-8199 | 20020417 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | EP 1354953 | A1 | 20031022 | EP 2002-15499 | 20020712 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| | WO 2003086470 | A2 | 20031023 | WO 2003-EP4039 | 20030417 |
| | WO 2003086470 | A3 | 20040506 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VZ, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRAI EP 2002-8199 A 20020417

EP 2002-15499 A 20020712

AB The invention is directed to the use of Smac to sensitize different tumors and self-reactive immune cells to various pro-apoptotic stimuli, in that the cells subsequently undergo apoptosis. Therefore, Smac can be used as a compound for the manufacture of a medicament for the treatment of cancer and autoimmune diseases. Sensitization of the cells is achieved either by applying a cell-permeable form of Smac combined with known anticancer agents or by overexpression of the protein. It is an object of the invention to provide a new method in cancer and autoimmune disease therapy by using Smac agonists for apoptosis regulation. Thus, Smac agonists represent novel promising cancer and autoimmune disease therapeutics to potentiate the efficacy of cytotoxic therapies even in resistant tumors and immune cells. In particular, overexpression of full-length Smac protein potentiated TRAIL-induced apoptosis and also markedly increased apoptosis induced by anti-CD95 antibody or cytotoxic drugs in transfected

SHEP neuroblastoma cells. The overexpression of Smac is shown to promote apoptosis through antagonizing the inhibition of XIAP of both distal and proximal events in the caspase cascade. The cytosolic Smac, with the deletion of transit peptide for mitochondria (N-terminal 55 AA), bypasses Bcl-2 inhibition in several cell types in response to different pro-apoptotic stimuli. The cell permeable Smac peptide (4 N-terminal IAP-interacting plus 3 addition following residues linked to TAT transduction domain) can facilitate intracellular delivery of Smac peptide and sensitize several resistant cell lines with defects in apoptosis signaling for treatment with TRAIL or doxorubicin. Expression of a cytosolic active form of Smac or cell-permeable Smac peptides bypassed the Bcl-2 block, which prevented the release of Smac from mitochondria, and also sensitized resistant neuroblastoma or melanoma cells and patient-derived primary neuroblastoma cells ex vivo. Thus, Smac agonists represent novel promising cancer therapeutics to potentiate the efficacy of cytotoxic therapies. Smac peptides is shown to enhance the antitumor effect of TRAIL in glioblastoma in mouse glioblastoma model and induce eradication of tumors.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:146167 CAPLUS
DN 139:131557

TI A Novel Ubiquitin Fusion System Bypasses the Mitochondria and Generates Biologically Active Smac/DIABLO

AU Hunter, Allison M.; Kottachchi, Dan; Lewis, Jennifer; Duckett, Colin S.; Korneluk, Robert G.; Liston, Peter

CS Children's Hospital of Eastern Ontario, Solange Gauthier Karsh Molecular Genetics Laboratory, Research Institute, Ottawa, ON, K1H 8L1, Can.

SO Journal of Biological Chemistry (2003), 278(9), 7494-7499
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB Smac/DIABLO is a mitochondrial protein that is proteolytically processed and released during apoptosis along with cytochrome c and other proapoptotic factors. Once in the cytosol, Smac protein binds to inhibitors of apoptosis (IAP) proteins and disrupts the ability of the IAPs to inhibit caspases 3, 7, and 9. The requirement for mitochondrial processing and release has complicated efforts to delineate the effect of Smac overexpression and IAP inhibition on cell death processes. In this report, we document a novel expression system using ubiquitin fusions to express mature, biol. active Smac in the cytosol of transfected cells. Processing of the ubiquitin-Smac fusions is rapid and complete and generates mature Smac protein initiating correctly with the Ala-Val-Pro-Ile tetrapeptide sequence that is required for proper function. The biol. activity of this exogenous protein was demonstrated by its interaction with X-linked IAP, one of the most potent of the IAPs. The presence of mature Smac was not sufficient to trigger apoptosis of healthy cells. However, cells with excess Smac protein were greatly sensitized to apoptotic triggers such as etoposide exposure. Cancer cells typically display deregulated apoptotic pathways, including Bcl2 overexpression, thereby suppressing the release of cytochrome c and Smac. The ability to circumvent the requirement for mitochondrial processing and release is critical to developing Smac as a possible gene therapy payload in cancer chemosensitization.

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:927451 CAPLUS
DN 138:19527

TI IAP binding peptides and assays for identifying compounds that bind IAP

IN McLendon, George; Kipp, Rachel A.; Case, Martin; Shi, Yigong
PA The Trustees of Princeton University, USA
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2002096930 | A2 | 20021205 | WO 2002-US17342 | 20020531 |
| | WO 2002096930 | A3 | 20040318 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
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| | EP 1421204 | A2 | 20040526 | EP 2002-729333 | 20020531 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | JP 2004531731 | T2 | 20041014 | JP 2003-500109 | 20020531 |
| PRAI | US 2001-294682P | P | 20010531 | | |
| | US 2002-345630P | P | 20020103 | | |
| | WO 2002-US17342 | W | 20020531 | | |

OS MARPAT 138:19527

AB Assays are disclosed for identifying peptides and peptidomimetics for promoting apoptosis in cells, through a pathway involving the Inhibitor of Apoptosis Proteins (IAPs), exemplified by XIAP, and the mitochondrial protein Smac/DIABLO (hereinafter Smac) and homologs thereof. The present invention features an assay for use in high throughput screening or rational drug design of agents that can, like the Smac tetrapeptide or its homologs in other species, bind to a BIR domain of an IAP, thereby relieving IAP-mediated suppression of apoptosis. The assay comprises the following basic steps: (a) providing a labeled mimetic of an IAP-binding tetrapeptide that binds to the appropriate BIR domain (preferably BIR3), wherein at least one measurable feature of the label changes as a function of the mimetic being bound to the IAP or free in solution; (b) contacting the BIR domain of an IAP with the labeled mimetic under conditions enabling binding of the mimetic to the BIR domain, thereby forming a BIR-labeled mimetic complex having the measurable feature; (c) contacting the BIR-labeled mimetic complex with the compound to be tested for BIR binding; and (d) measuring displacement of the labeled mimetic from the BIR-labeled mimetic complex, if any, by the test compound, by measuring the change in the measurable feature of the labeled mimetic, thereby determining if the test compound is capable of binding to the IAP. In a preferred embodiment, the labeled mimetic is AVPX, wherein X is directly or indirectly linked to a fluorogenic dye. Preferably, it is AVPC attached to a badan dye. The present invention also provides a library of peptides or peptidomimetics that have been demonstrated by the methods of the invention to bind to the BIR3 domain of XIAP.

L3 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:293679 CAPLUS
DN 136:305833

TI Peptides derived from smac (DIABLO) and methods of using them to screen for apoptosis modulating compounds

IN Fesik, Stephen W.; Meadows, Robert P.; Betz, Stephen P.; Liu, Zhihong; Olejniczak, Edward T.; Sun, Chaohong

PA Abbott Laboratories, USA

SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|------|----------|-----------------|----------|
| PI | WO 2002030959 | A2 | 20020418 | WO 2001-US32121 | 20011012 |
| | WO 2002030959 | A3 | 20020926 | | |

W: CA, JP, MX

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, TR

PRAI US 2000-687549 A 20001013

AB The present invention relates to peptides derived from the wild-type human smac (DIABLO) protein which binds to a member of an IAP (inhibitor-of-apoptosis protein) family member, which regulate programmed cell death by inhibiting members of the caspase family of enzymes. The peptides of the present invention can be used in an assay to identify candidate substances which induce or promote apoptosis in cells. These IAP-binding peptides are derived from the 9-amino acid N-terminal smac (DIABLO) protein which have the amino acid sequence: Ala-Xaax-Xaay-Xaaz-(Xaa)n-B, wherein Xaax, Xaay, and Xaaz, each represent a hydrophobic amino acid independently selected from the group consisting of leucine, valine, isoleucine, phenylalanine, proline, tryptophan, tyrosine, and methionine, n independently has a value from 0 to 20, where at least one of the Xaan amino acids is the same or different from that of the wild-type human smac (DIABLO) protein, and B is absent or is a carboxy protecting group.

L3 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:256295 CAPLUS

DN 136:289086

TI Compositions and methods for regulating apoptosis

IN Shi, Yigong

PA Trustees of Princeton University, USA

SO PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|------|----------|-----------------|----------|
| PI | WO 2002026775 | A2 | 20020404 | WO 2001-US30567 | 20010928 |
| | WO 2002026775 | A3 | 20030123 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001093189 A5 20020408 AU 2001-93189 20010928

US 2002177557 A1 20021128 US 2001-965967 20010928

PRAI US 2000-236574P P 20000929

US 2000-256830P P 20001220

WO 2001-US30567 W 20010928

OS MARPAT 136:289086

AB Peptides and peptidomimetics capable of modulating apoptosis through their interaction with cellular IAPs (inhibitor of apoptosis proteins) are disclosed. The peptides and mimetics are based on the N-terminal tetrapeptide of IAP-binding proteins, such as Smac/DIABLO, Hid, Grim and Reaper, which interact with a sp. surface groove of IAP. Also disclosed are methods of using these peptides and peptidomimetics for therapeutic purposes and for rational drug design.

L3 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:157823 CAPLUS
DN 136:212574
TI Protein Smac and its functional variants, their function in promoting
apoptosis and uses in identifying modulators of apoptosis
IN Alnemri, Emad S.
PA Thomas Jefferson University, USA
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|------|----------|--|----------|
| PI | WO 2002016418 | A2 | 20020228 | WO 2001-US26492 | 20010824 |
| | WO 2002016418 | A3 | 20030206 | | |
| | W: | | | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | |
| | RW: | | | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | |
| | AU 2001086730 | A5 | 20020304 | AU 2001-86730 | 20010824 |
| | EP 1315811 | A2 | 20030604 | EP 2001-966195 | 20010824 |
| | R: | | | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | |

PRAI US 2000-227735P P 20000824
WO 2001-US26492 W 20010824

AB The present invention discloses that sequences of isolated DNA mols. encoding cytosolic isoform of Smac and its function variants, in particular, the N-terminus of the protein, which are capable of specifically binding to at least a portion of an inhibitor of apoptosis protein (IAP) protein and promoting apoptosis. In particular, the invention discloses that protein Smac has at least two contiguous amino acid residues derived from at least residues 56-139 of SEQ ID NO: 1 and of which up to 184 contiguous amino acid residues can be derived from residues 56-239 of SEQ ID NO: 1, a functional variant of each or a functional equivalent of each, each of which is capable of specifically binding to an IAP. The invention also relates to expression vectors that contains the DNA mols. of the present invention, host cells transformed with the expression vectors, antibodies to this protein as well as methods for inducing apoptosis in cells. The invention further discloses that this protein can be used in a method to modulate apoptosis or to identify modulators of apoptosis as well as in therapeutic uses.

L3 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:157809 CAPLUS
DN 136:210550
TI Apoptotic peptide compounds interacting with inhibitor of apoptosis
protein for pathogenic cell apoptosis
IN Wang, Xiaodong; Du, Chunying
PA Board of Regents, the University of Texas System, USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|------|----------|-----------------|----------|
| PI | WO 2002016402 | A2 | 20020228 | WO 2001-US41869 | 20010823 |
| | WO 2002016402 | A3 | 20020613 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
 PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
 UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 6608026 B1 20030819 US 2000-645075 20000823
 AU 2001091270 A5 20020304 AU 2001-91270 20010823
 US 2004077542 A1 20040422 US 2003-641539 20030815
 PRAI US 2000-645075 A 20000823
 WO 2001-US41869 W 20010823

OS MARPAT 136:210550

AB The invention provides methods and compns. for apoptosis of pathogenic cells. The general method comprises contacting the cells with an effective amount of an AV peptoid, wherein the AV peptoid is a peptide comprising AX1, wherein X1 is V, I or L, or a peptide mimetic thereof, which interacts with an Inhibitor of Apoptosis protein (IAP) as measured by IAP binding, procaspase-3 activation or promotion of apoptosis, wherein apoptosis of the pathogenic cells is enhanced. The subject compns. encompass pharmaceutical compns. comprising a therapeutically effective amount of a subject AV peptoid in dosage form and a pharmaceutically acceptable carrier, wherein the AV peptoid is a peptide comprising AX1, wherein X1 is V, I or L, or a peptide mimetic thereof, which inhibits the activity of an Inhibitor of Apoptosis protein (IAP) as measured by IAP binding, procaspase-3 activation or promotion of apoptosis. The invention also provides assays for identifying agents which modulates the interaction of an AV peptoid with an IAP, active compds. identified in such screens and their use in the foregoing compns. and therapeutic methods. Both peptoid and chemotherapies demonstrated inhibition of human lung large cell carcinomas in mice; combination therapies provided enhanced inhibition over either therapy alone.

L3 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:833504 CAPLUS

DN 137:358061

TI Conserved sequence of XIAP-binding motif in human caspase-9 and Smac/DIABLO and therapeutic uses for screening modulators of apoptosis

IN Alnemri, Emad S.

PA Thomas Jefferson University, USA

SO U.S. Pat. Appl. Publ., 52 pp., Cont.-in-part of U.S. Ser. No. 939,293.
 CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|------|----------|-----------------|----------|
| PI | US 2002160975 | A1 | 20021031 | US 2002-68569 | 20020206 |
| | US 2002132786 | A1 | 20020919 | US 2001-939293 | 20010824 |
| | WO 2003010184 | A2 | 20030206 | WO 2002-US3553 | 20020206 |
| | WO 2003010184 | A3 | 20030814 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
 GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
 GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-267966P P 20010208

US 2001-939293 A2 20010824
US 2000-227735P P 20000824

AB The invention provides conserved sequence of XIAP-binding motif in human caspase-9 and Smac/DIABLO. The invention also provides caspase-9-related peptides and polypeptides capable of binding to an Inhibitor of Apoptosis Protein (IAP), as well as caspase-9 mutant that fail to undergo normal processing and fail to bind to an IAP. Nucleic acid mols., including expression vectors, encoding such peptides and polypeptides are also provided. Such peptides and polypeptides, are useful for inducing apoptosis and identifying inhibitors and enhancer of apoptosis.

L3 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:363320 CAPLUS
DN 137:105391

TI Molecular Targeting of Inhibitor of Apoptosis Proteins Based on Small Molecule Mimics of Natural Binding Partners

AU Kipp, Rachael A.; Case, Martin A.; Wist, Aislyn D.; Cresson, Catherine M.; Carrell, Maria; Griner, Erin; Wiita, Arun; Albiniaak, Philip A.; Chai, Jijie; Shi, Yigong; Semmelhack, Martin F.; McLendon, George L.

CS Department of Chemistry, Frick Laboratory and Department of Molecular Biology, Lewis Thomas Laboratory, Princeton University, Princeton, NJ, 08544, USA

SO Biochemistry (2002), 41(23), 7344-7349
CODEN: BICHAW; ISSN: 0006-2960

PB American Chemical Society

DT Journal

LA English

AB An assay based on a solvent-sensitive fluorogenic dye mol., badan, is used to test the binding affinity of a library of tetrapeptide mols. for the BIR3 (baculovirus IAP repeat) domain of XIAP (X-linked inhibitor of apoptosis protein). The fluorophore is attached to a tetrapeptide, Ala-Val-Pro-Cys-NH₂, through a thiol linkage and, upon binding to XIAP, undergoes a solvatochromic shift in fluorescence emission. When a mol. (e.g., a natural protein known to bind to XIAP or a tetrapeptide mimic) displaces the dye, the emission shifts back to the spectrum observed in water. As emission intensity is related to the binding of the tetrapeptide, the intensity can be used to determine the equilibrium constant,

K, for the displacement of the dye by the tetrapeptide. The results permit residue-specific anal. of the interaction. Furthermore, we show that hydrophobic effects in the fourth position are general and can effectively increase overall affinity.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
AN 1991:409096 CAPLUS
DN 115:9096

TI Cyclopeptide alkaloids: further studies on mauritine-C and sativanine-C

AU Shah, A. H.; Al-Yahya, M. A.; El-Sayed, A. M.; Tariq, M.; Ageel, A. M.

CS Coll. Pharm., King Saud Univ., Riyadh, 11451, Saudi Arabia

SO Pakistan Journal of Pharmaceutical Sciences (1989), 2(2), 81-9
CODEN: PJPSEN; ISSN: 1011-601X

DT Journal

LA English

AB The 14-membered cyclopeptide alkaloid mauritine-C (I) and the 13-membered cyclopeptide alkaloid sativanine-C were isolated from Zizyphus spinea-christi and Zizyphus sativa commonly used in the Saudi Folklor medicine. The N-formyl derivs. of these compds. were prepared and their corresponding spectral data was analyzed. Fundamental differences were observed in the mass spectrometric fragmentation of the newly formed derivs. as compared to the parent compds. High resolution mass spectrometry was found a useful tool to substantiate the fragmentation pattern proposed for these potential natural products.

L3 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1987:153052 CAPLUS
 DN 106:153052
 TI The alkaloids of *Zizyphus sativa*
 AU Shah, A. H.; Miana, G. A.; Tschesche, R.
 CS Dep. Chem., Gomal Univ., D. I. Khan, Pak.
 SO Nat. Prod. Chem., Proc. Int. Symp. Pak.-U.S. Binatl. Workshop, 1st (1986),
 Meeting Date 1984, 404-29. Editor(s): Rahman, Atta Ur. Publisher:
 Springer, Berlin, Fed. Rep. Ger.
 CODEN: 55JSAT
 DT Conference
 LA English
 AB Chromatog. of the bark of *Z. sativa* yielded the alkaloids frangufoline,
 nummularine B, mucronine D, and the sativanines A-G. Identification of
 the compds. was made from mass spectral data.

L3 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1986:65887 CAPLUS
 DN 104:65887
 TI The alkaloids of Rhamnaceae. Part 39. An N-formyl cyclopeptide alkaloid
 from the bark of *Zizyphus sativa*
 AU Shah, A. H.; Pandey, V. B.; Eckhardt, G.; Tschesche, R.
 CS Dep. Chem., Gomal Univ., Dera Ismail Khan, Pak.
 SO Phytochemistry (Elsevier) (1985), 24(11), 2768-70
 CODEN: PYTCAS; ISSN: 0031-9422
 DT Journal
 LA English
 AB From the bark of *Z. sativa*, a previously undescribed cyclopeptide
 alkaloid, sativanine F (I) was isolated. The structure was deduced by
 spectroscopic methods and chemical degradation. It is a 13-membered
 cyclopeptide
 alkaloid and provides the first example of such a naturally occurring
 N-formyl cyclopeptide alkaloid.

L3 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
 AN 1984:587941 CAPLUS
 DN 101:187941
 TI The alkaloids of Rhamnaceae. Part 34. Sativanine C: a cyclopeptide
 alkaloid from the bark of *Zizyphus sativa*
 AU Shah, A. H.; Pandey, V. B.; Eckhardt, G.; Tschesche, R.
 CS Dep. Chem., Gomal Univ., D. I. Khan, Pak.
 SO Phytochemistry (Elsevier) (1984), 23(4), 931-3
 CODEN: PYTCAS; ISSN: 0031-9422
 DT Journal
 LA English
 AB Sativanine-C (I) was isolated from *Z. sativa* and its structure was determined
 by standard chemical and spectral methods.